Initial REMS approval: 02/2013
Most recent modification: 06/2015

Buprenorphine-containing Transmucosal products for Opioid Dependence (BTOD)
Risk Evaluation and Mitigation Strategy (REMS)

This REMS applies to buprenorphine-containing oral transmucosal products indicated for the treatment of opioid dependence (hereinafter, "buprenorphine-containing products"). This REMS does not apply to buprenorphine-containing products that are dispensed to patients admitted to an Opioid Treatment Program under 42 CFR Part 8.

I. Goals:

The goals of the Buprenorphine-containing Transmucosal products for Opioid Dependence (BTOD) REMS are to:

- Mitigate the risks of accidental overdose, misuse, and abuse
- Inform prescribers, pharmacists, and patients of the serious risks associated with buprenorphine-containing products

II. REMS ELEMENTS:

A. Medication Guide

A Medication Guide for Trade name (MG) will be dispensed with each prescription for a buprenorphine-containing product in accordance with 21 CFR 208.24.

The Medication Guides for buprenorphine-containing products are part of the BTOD REMS and will be available through the BTOD REMS website (www.btodrems.com).

B. Elements to Assure Safe Use

1. Safe use conditions

a. Buprenorphine-containing products will only be dispensed by the prescriber or prescribed to patients with documentation of the following safe use conditions:

   i. Verification that the patient meets the diagnostic criteria for opioid dependence.

   ii. Risks described in the professional labeling and the Medication Guide have been discussed with the patient.

   iii. Safe storage of the medication has been explained and reviewed with the patient.

   iv. After appropriate induction, the patient is prescribed a limited amount of medication at the first visit.

b. Prescribers will document safe use conditions for each patient by using the 'Appropriate Use Checklist,' or by using another method (e.g. electronic health record) specific to the prescriber's office practice.

c. Sponsors of this waiver-granted shared REMS (BTOD Sponsors) will ensure that within 60 days of FDA approval of the BTOD REMS, a Dear Prescriber Letter will be mailed to all prescribers certified to treat opioid dependence under the Drug Addiction Treatment Act of 2000 (DATA 2000). This letter is designed to convey and reinforce the risks of accidental overdose, misuse, and abuse of buprenorphine-containing products, as well as the need to appropriately monitor patients and document safe use conditions. The prescriber brochure, *Office-Based Buprenorphine Therapy for Opioid Dependence: Important Information for Prescribers*, and the Appropriate Use Checklist will be appended to the Dear Prescriber Letter. The letter will provide instructions on where to obtain copies of the Full Prescribing Information and Medication Guides. Mailings will occur annually thereafter.

d. BTOD Sponsors will, on a monthly basis, identify any newly DATA 2000-certified prescribers and mail the applicable documents to them. The prescriber brochure, *Office-Based Buprenorphine Therapy for Opioid Dependence: Important Information for Prescribers* and the Appropriate Use Checklist will be appended to the Dear Prescriber Letter. The letter will provide instructions on where to obtain copies of the Full Prescribing Information and Medication Guides.

e. To further reinforce safe use conditions, BTOD Sponsors will ensure that within 60 days of FDA approval of the BTOD REMS, a Dear Pharmacist Letter will be mailed to all retail pharmacies authorized by DEA to handle schedule III controlled substances on a national mailing list from the National Technical Information Service. The pharmacist brochure, *Office-Based Buprenorphine Therapy for Opioid Dependence: Important Information for Pharmacists* will be appended to the Dear Pharmacist Letter. The letter will provide instructions on where to obtain copies of the Full Prescribing Information and Medication Guides. Mailings will occur annually thereafter.

f. BTOD Sponsors will make the letters and all materials that are appended to the letters available through its toll-free information line, through BTOD REMS specialists and on the BTOD REMS website.

g. On a monthly basis, the BTOD REMS specialists will make attempts to contact all newly certified prescribers listed on the SAMHSA website and a random sample of existing prescribers via outbound call center calls.

1. The BTOD REMS specialists will create awareness of the program, confirm that REMS materials have been received by the prescriber, and confirm understanding of the BTOD REMS requirements.
2. The BTOD REMS specialists will mail a copy of the REMS materials to prescribers who did not receive or request the REMS materials.
3. The BTOD REMS specialists will offer to provide additional follow-up information. If further follow-up is requested, the BTOD REMS specialist will offer the following options:
    - Option I: A BTOD REMS specialist will provide a live online meeting to review BTOD REMS requirements
    - Option II: A BTOD REMS specialist will provide a field visit to review BTOD REMS requirements

2. Monitoring

a. Each patient using a buprenorphine-containing product will be subject to the following monitoring:

i. Return visits are scheduled at intervals commensurate with patient stability. Weekly, or more frequent, visits are recommended for the first month.

ii. Assessment and reinforcement of patient's compliance with the prescribed medication.

iii. Assessment of appropriateness of dosage prescribed.

iv. Assessment of whether patient is receiving the necessary psychosocial support.

v. Assessment of whether patient is making adequate progress towards treatment goals.

b. Prescribers will document that each patient has received the required clinical monitoring using the 'Appropriate Use Checklist,' or by using another method/system (e.g. electronic health record) specific to the prescriber's office practice.

The following materials are part of the BTOD REMS and are appended to the REMS document:

- Dear Prescriber Letter
- Dear Pharmacist Letter
- Appropriate Use Checklist
- Prescriber Brochure, *"Office-Based Buprenorphine Therapy for Opioid Dependence: Important Information for Prescribers"*
- Pharmacist Brochure, *"Office-Based Buprenorphine Therapy for Opioid Dependence: Important Information for Pharmacists"*
- BTOD REMS Website (www.btodrems.com)

C. Implementation System

BTOD Sponsors will:

- Ensure that all DATA 2000-certified prescribers receive the Dear Prescriber Letter with the appended materials.
- Monitor compliance with the prescriber requirements to document prescribing and dispensing with documentation of safe use conditions through surveys of patients and prescribers, evaluations of health care utilization databases, and ongoing surveillance (sources including, but not limited to, internet, national databases, and surveys conducted at substance abuse treatment programs).
- Monitor and evaluate the implementation of the elements to assure safe use provided for under Sections B1, above, and in the manner described in the REMS supporting document, and take reasonable steps to improve implementation of these elements to meet the goals of the BTOD REMS, if the goals of the REMS are not being met.

D. Timetable for Submission of Assessments

The BTOD submission of assessments occurs annually with a due date of August 30th, beginning in 2014. To facilitate inclusion of as much information as possible, while allowing reasonable time to prepare the submission, the reporting interval covered by each assessment will conclude no earlier than 60 days before the submission date for that assessment. The NDA holder(s) will submit each assessment so that it will be received by the FDA on or before the due date.